BEST AVAILABLE COPY

```
d his

     (FILE 'USPAT' ENTERED AT 07:44:43 ON 30 SEP 91)
                SET PAGELENGTH 19
30 SEP 91 07:56:17            U.S. Patent & Trademark Office            P0008
                SET LINELENGTH 78
L1              1 S MEMORY AND DATA CURVE AND PHASE CHARACTERISTIC#
L2              1 S L1 AND COMPUTER AND PROBE# AND COMPAR###
L3          57852 S COMPUTER AND COMPAR####
L4             73 S PHASE CHARACTERISTIC# AND PROBE#
L5             52 S FLUID AND DATA CURVE#
L6              1 S L3 AND L4 AND L5
L7             24 S L3 AND L4
L8              4 S L7 AND FLUID#

=> d l8 1-4 cit

1.  4,774,680, Sep. 27, 1988, Method and apparatus for net oil measurement;
Joram Agar, 364/550; 73/61.1R, 861.04; 324/71.1, 698

2.  4,739,521, Apr. 19, 1988, Medical image diagnostic system; Taizo Akimoto,
359/143; 354/131; 358/244; 359/173 [IMAGE AVAILABLE]
30 SEP 91 07:57:16            U.S. Patent & Trademark Office            P0009

3.  4,713,347, Dec. 15, 1987, Measurement of ligand/anti-ligand interactions
using bulk conductance; David H. Mitchell, et al., 436/501; 204/403; 324/439,
692; 422/82.02; 435/6, 291, 311; 436/30, 149, 527, 533, 806, 807; 935/78
[IMAGE AVAILABLE]

4.  3,908,933, Sep. 30, 1975, Guided missile; Wilbur H. Goss, et al.,
244/3.21; 60/270.1 [IMAGE AVAILABLE]

=>




d his

     (FILE 'USPAT' ENTERED AT 07:44:43 ON 30 SEP 91)
                SET PAGELENGTH 19
                SET LINELENGTH 78
L1              1 S MEMORY AND DATA CURVE AND PHASE CHARACTERISTIC#
L2              1 S L1 AND COMPUTER AND PROBE# AND COMPAR###
L3          57852 S COMPUTER AND COMPAR####
L4             73 S PHASE CHARACTERISTIC# AND PROBE#
30 SEP 91 08:12:37            U.S. Patent & Trademark Office            P0032
L5             52 S FLUID AND DATA CURVE#
L6              1 S L3 AND L4 AND L5
L7             24 S L3 AND L4
L8              4 S L7 AND FLUID#
L9              2 S L8 AND DATA
L10             4 S L8 AND (DATA OR VALUE# OR NUMBER#)

=> d l10 cit 1-4

1.  4,774,680, Sep. 27, 1988, Method and apparatus for net oil measurement;
Joram Agar, 364/550; 73/61.1R, 861.04; 324/71.1, 698

2.  4,739,521, Apr. 19, 1988, Medical image diagnostic system; Taizo Akimoto
```

359/143; 354/131; 358/244; 359/173 [IMAGE AVAILABLE]

3. 4,713,347, Dec. 15, 1987, Measurement of ligand/anti-ligand interactions using bulk conductance; David H. Mitchell, et al., 436/501; 204/403; 324/439,

692; 422/82.02; 435/6, 291, 311; 436/30, 149, 527, 533, 806, 807; 935/78 [IMAGE AVAILABLE]

4. 3,908,933, Sep. 30, 1975, Guided missile; Wilbur H. Goss, et al., 244/3.21; 60/270.1 [IMAGE AVAILABLE]

=> d l10 1-4 kwic

US PAT NO: 4,774,680 L10: 1 of 4

ABSTRACT:
Disclosed . . . the oil/water mixture yields a current output which can be plotted on one of two distinct, empirically or theoretically derived, data curves. One of the data curves represents oil being in the continuous phase and the other data curve represents water being in the continuous phase. A comparator is used to determine whether the oil or the water is in the continuous phase to thereby select the proper data

US PAT NO: 4,774,680 L10: 1 of 4
curve on which the energy absorption is plotted. Each of the curves has the energy absorption properties of the media. . .

SUMMARY:

BSUM(5)

There are in the prior art a number of instruments which have been used to measure water content in an oil/water mixture. Most of such instruments in the. . .

SUMMARY:

BSUM(6)

US PAT NO: 4,774,680 L10: 1 of 4

BSUM(6)
A relatively typical capacitance probe for use in determining oil/water ratios is found in U.S. Pat. No. 3,200,312 to Callahan. Callahan relies on the measurement of the mixture's dielectric constant. As such, the probe must be non-functional when water is in the continuous phase.

SUMMARY:

BSUM(7)

Yet another capacitance-type probe is taught in U.S. Pat. No. 3,025,464 to Bond. The Bond probe is designed specifically for pipeline use where there is typically low water content and oil is in the continuous phase. For that purpose, the Bond probe will function adequately. However, because

US PAT NO: 4,774,680 L10: 1 of 4

BSUM(7)
the Bond probe is a capa ance probe, it will not ction in mixtures where water becomes the continuous phase.

SUMMARY:

BSUM(8)

Still another prior art capacitance probe is shown in U.S. Pat. No. 3,523,245 to Love et al. It has the same shortcomings as the prior art. . . references mentioned above. In fact, FIG. 2 of the Love et al patent depicts a graph for water fraction versus probe capacitance. It is noted that the water fraction portion of the graph does not go above Ø.5. In fact, the. . . that when the water fractions get above Ø.5, the water tends to separate

BSUM(8)
out and the capacitance quickly approaches the value at free water.

SUMMARY:

BSUM(11)

Yet another net oil computer is described in U.S. Pat. No. 3,385,1Ø8 to Rosso. Rosso relies on a capacitance probe and does not teach the use of a digital linearizer or any means of overcoming the jump in the electrical. . .

SUMMARY:

BSUM(12)

Another typical capacitance probe having the same inadequacies as those probes mentioned above is found in U.S. Pat. No. 3,ØØ6,189 to Warren et al.

SUMMARY:

BSUM(21)

Briefly . . . detailed description, claims and drawings set forth hereinafter. These features, objects and advantages are accomplished by utilizing a microprocessor or comparator circuit which is able to distinguish between oil being in the continuous phase and water being in the

BSUM(21)
continuous phase. . .

SUMMARY:

BSUM(22)

As noted earlier, the step jump occurs in the data when the mixture changes over from oil being in the continuous phase to water being in the continuous phase. It is very desirable to eliminate this step jump from the data and to linearize the two distinct curves.

SUMMARY:

BSUM(23)

It . . . a conductivity meter or energy absorption detector usually in units of milliamps of output. This information is fed to a comparator to select one of two memories, those being where water is in the continuous phase and where oil is in. . .

DRAWING DESC:

DRWD(2)

FIG. 1 is an elevational view of a probe and oil/water monitor as used in conjunction with the present invention.

DRWD(2)

DRAWING DESC:

DRWD(3)

FIG. 2 is a schematic diagram of the flow of data through the apparatus of the present invention.

DETDESC:

DETD(2)

Turning first to FIG. 1 and there is shown a probe 10 mounted within a

DETD(2)
conduit 12. Energy is transmitted into the medium from oil/water monitor 14 through probe 10. In such manner, oil/water monitor 14 can measure the electrical properties of the media flowing through conduit 12. Typically,. . .

DETDESC:

DETD(4)

The . . . the continuous phase to water being in the continuous phase. Because the location of the step is affected by a number of variables, it can be difficult to determine precisely what pecentage of water is present.

DETD(4)

DETDESC:

DETD(7)

Still . . . current generator 15, a capacitor 17 and an ammeter 19. The capacitor 17 should be in the form of a probe inserted into the fluid. The ammeter 19 measures current [I]so that when water is in the continuous phase the circuit can be defined by. . .

DETDESC:

DETD(12)

where "j" is the square root of -1, "w" represents the radial frequency and "c" represents capacitance of the probe with the mixture inside it. Thus there can be theoretically derived two distinct curves or equations representing some electrical property. . .

DETDESC:

DETD(16)

where . . . is in the continuous phase. As mentioned earlier, the constituent which is in the continuous phase is affected by a number of other variables. Therefore, it is probably simpler to use the empirically generated curves shown in FIG. 3.

DETD(16)

DETDESC:

DETD(17)

The . . . 16 which allows the device of the present invention to be calibrated. From the zero to span adjuster 16 the data is transmitted to an analog to digital converter 18 and to a comparator 20. The comparator 20 uses this information to select one of two memories. There is a continuous water phase memory 22 and a. . .

DETDESC:

DETD(18)

The . . . have been projected past the points where they intersect the step jump 27 as shown by the dashed lines. The comparator 20 is, in actuality, a microprocessor or other computing device which compares the measured electrical signal shown in FIG. 3 as current with a preset value, say 5 milliamps. If the measured current is greater than the preset value, then water is in the continuous phase and the comparator 20 selects water continuous phase memory 22 with data plotted as the upper milliamperage curve 23. If the measured current is less than the preset value, then the oil is in the continuous phase and the comparator 20 selects oil continuous phase memory 24 containing data plotted as the lower milliamperage curve 25.

DETD(18)

DETDESC:

DETD(19)

The data transmitted from the oil/water monitor 14 provides the comparator 20 with the amount of current measured so that the comparator 20 can compare that value to the preset value.

DETDESC:

DETD(20)

US PAT NO: 4,774,680 L10: 1 of 4

DETD(20)
Depending on which continuous memory 22 or 24 is selected, the data is transmitted from analog to digital converter 18 to that particular phase memory 22 or 24 where the amount of. . . current is used to determine the percentage of water present by way of curve 23 or curve 25. The digitized data representing the percentage of water present is then transmitted to multiplier 26 and simultaneously, to a digital to analog converter 28. The data from the digital to analog converter 28 is then transmitted to a meter 30 where the percent of water can. . .

DETDESC:

DETD(21)

US PAT NO: 4,774,680 L10: 1 of 4

DETD(21)
The . . . 36. Gross flow totalizer 36 keeps a running tabulation of the total volume pumped through conduit 12. The gross flow data transmitted from flow meter 32 to multiplier 26 is multiplied by the percentage of water data transmitted to multiplier 26 from memories 22 and 24. The data is then transmitted from multiplier 26 simultaneously to net water totalizer 38 and to subtractor 34. Net water totalizer 38. . .

DETDESC:
=> d l10 2-4 kwic

US PAT NO: 4,739,521 [IMAGE AVAILABLE] L10: 2 of 4

SUMMARY:

US PAT NO: 4,739,521 [IMAGE AVAILABLE] L10: 2 of 4

BSUM(3)

Recently, . . . medical diagnostic systems, there has been known a system including a device for processing an image signal transferred from a computer tomography apparatus (X-ray CT) or a nuclear magnetic resonance computer tomography apparatus (NMRCT) using a computer to thereby obtain a clear image of a portion of the patient's body. The system further includes a device responsive. . .

SUMMARY:

BSUM(4)

For . . . magnetic resonance (which has the advantage of no radiation

US PAT NO: 4,739,521 [IMAGE AVAILABLE] L10: 2 of 4

BSUM(4)
hazard) and which is particularly suitable for detecting the state of fluids in the patient's body.

SUMMARY:

BSUM(8)

Further, there is a nee for the image density to made greater, for example, by increasing t number of scanning lines om about 500 to about 1000. In such a case, a sufficient bandwidth cannot be obtained using ordinary high-frequency cables. Moreover, the phase characteristics of the image signal are such that, in the case where the video converting circuit, the image display device, and. . .

BSUM(8)

DETDESC:

DETD(3)

In . . . it is possible to use known devices, for example, the scintillator and photomultiplier of an X-ray CT system, a the probe head of an NMR-CT system, or the image intensifier of an X-ray system.

DETDESC:

DETD(4)

DETD(4)

The . . . in which image processing such as image reconstruction, gradation conversion, frequency enhancement, addition/subtraction, and the like are performed by a computer. The output of the device 30 is applied to a video signal converting circuit 40 and is converted thereby into. . .

DETDESC:

DETD(10)

Further, . . . other hand, the O/E converter can be constituted of a light-detecting element (for example, a photo diode), an amplifier, a comparator, and a level converting circuit. Light entering the O/E converter through an optical fiber is converted into a current signal by the

DETD(10)

photo diode or the like, amplified using the amplifier, compared by the comparator, and converted to have a level satisfying predetermined interface conditions.

DETDESC:

DETD(18)

In . . . for example, loading of a film cassette or a power switch, a photography switch 62 for performing exposure, a frame number setting switch 63 for selecting the number of frames to be recorded on the sheet of film, a photographic order setting switch 64 for selecting the order. . . unit 82 for indicating a selected photography condition channel, an

DETD(19)

indicator unit 83 for indicting a set photographic format (the number of photographic frames, the photographing order, etc.), an indicator unit 84 for indicating the number of available photographic films, an indicator unit 85 for indicating the number of photographic frames, a brightness value indicator unit 86, a contrast value indicator unit 87, and a negative/positive indicator unit 88.

DETDESC:

DETD(20)

Referring . . . an image of 1000 or more scanning lines per screen both electro-optically and opto-electrically, and which have improved frequency

US PAT NO: 4,739,521 [IMAGE AVAILABLE] L10: 2 of 4

DETD(20)
and phase characteristics.

DETDESC:

DETD(25)

An optical fiber cable thus-manufactured was compared with conventional high-frequency cables, and the results described in the table below were obtained.

DETDESC:

US PAT NO: 4,739,521 [IMAGE AVAILABLE] L10: 2 of 4

DETD(27)

In order to corroborate these characteristics, a video signal containing a large number of scanning lines, such as 1084/60 Hz, was transmitted through E/O and O/E converters connected at the opposite ends of. . . a length of 1 km. It was found that no attenuation in the high frequency band an no variation in phase characteristics could be measured in the cable according to the present invention, and hence the image at the transmitter side could. . .

DETDESC:

DETD(38)

US PAT NO: 4,739,521 [IMAGE AVAILABLE] L10: 2 of 4

DETD(38)
(b) . . . device is provided on the console side, it is possible to perform photography more surely so as to reduce the number of photography failures.

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

ABSTRACT:
Methods, apparatus and sensors are described for detection of specific ligands in a fluid sample by measuring ligand-specific changes in the bulk electrical conductance (or resistance) of a fixed test volume, with antiligand or. . .

SUMMARY:

BSUM(2)

This . . . analytical methods and apparatus, more particularly to methods, apparatus and sensors for detection of a substance of interest in a fluid sample.

SUMMARY:

BSUM(3)

There are many types of standard tests or assays for detection of the presence and/or concentration of specific substances in fluids. Until

BSUM(3)

recently many of these assays required development of different reagents and protocols for each substance to be detected. Examples. . .

SUMMARY:

BSUM(4)

In . . . or assay has gained increasing use--the antibody-based assay, or immunoassay. In immunoassays, an antibody may be used, for example, to probe for the presence of a particular antigen, hapten, or other molecule. Immunoassays have several potential advantages over previous assays.

BSUM(4)

SUMMARY:

BSUM(8)

Immunoassays . . . have formed. As used herein, ligand is defined as the substance to be detected, and antiligand the substance used to probe for the presence of the ligand. (In some ligand/antiligand assays, an additional, perhaps modified, ligand may be used that competes. . .

SUMMARY:

BSUM(10)

Yet another ligand/antiligand assay that is becoming increasingly important is the nucleic acid hybridization assay, e.g., the DNA probe assay, which uses a "probe" strand of nucleic acid as an antiligand to test for the presence of a complementary DNA sequence. DNA probe assays, like immunoassays, often use radioactive labels, fluorescent labels or enzyme labels.

SUMMARY:

BSUM(11)

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(11)
spheres agglutinate due to antigen-antibody interaction. Both immunoassays and DNA probe assays have used luminescent labels as well.

SUMMARY:

BSUM(13)

A number of techniques are in commercial use or under development that seek to avoid some of the problems noted above by avoiding the use of labels or by modifying how lables are used. Many such techniques probe for the formation of ligand/antiligand complexes by optical means. For example, rate nephelometry, a type of immunoassay, measures changes in. . .

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(13)

SUMMARY:

BSUM(14)

Pregnancy . . . the lack of potential for continuous measurement or for making simultaneous determinations of multiple ligands in the same sample. A number of other immunoassay systems use some form of optical detection without relying on precipitin formation, agglutination or standard labels. See. . .

SUMMARY:

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(15)

There . . . 4,191,739, which makes a bulk conductance measurement. This technique is a modification of the Coulter counter approach, whereby a conducting fluid containing nonconducting particles is passed through a narrow constricted channel, whose overall (bulk) resistance is measured. The overall resistance increases. . . coated with antibody, for example, are exposed to antigen under appropriate conditions, they will aggregate, and the increased size and number of the aggregates can be related to the amount of antigen present. However, the sensitivity of this technique is limited. . . is attached), and it cannot easily be adapted to measure multiple ligands at the same time in a single sample fluid, nor to measure a continuously varying sample.

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(15)

SUMMARY:

BSUM(16)

U.S. . . . of a piezoelectric oscillator that has been coated with antigen to detect the presence of antigen or antibody in a fluid sample. More specifically, there is a change in the frequency of the oscillator as its mass changes due to binding. . . or sophisticated instrumentation; as

solution after exposure to the fluid sample and drying it before measurements can be made

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(16)

SUMMARY:

BSUM(20)

It . . . in less than a minute), capable of being continuous, capable of detecting the presence of multiple ligands simultaneously in a fluid sample, simple to perform and label-independent. It would also be advantageous to have an apparatus which enables such an assay. . .

SUMMARY:

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(22)

In . . . with the present invention, there are provided methods, apparatus and sensors for determining the presence of a ligand in a fluid sample by measuring changes in the bulk electrical conductance of a test volume. The conductance changes are made ligand-specific by. . . near the test volume of a predetermined region containing localized antiligand or ligand. This predetermined region is exposed to the fluid sample, ligand/antiligand interaction occurs, and the resulting conductance changes are monitored by any suitable conductance-measuring instrument.

SUMMARY:

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(23)

This invention also relates to methods and apparatus for eliminating non-specific noise and drift by (i) comparing the bulk conductance of a test volume with nearby negative or positive control volumes, and/or (ii) minimizing effects of phenomena. . .

SUMMARY:

BSUM(24)

More specifically, in one embodiment, the fluid sample flows through a predetermined region consisting of a matrix on which antiligand or ligand is immobilized. A suitable control. . .

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

BSUM(24)

DRAWING DESC:

DRWD(2)

FIG. 1A shows the change in the conductance ratio between a test sensor and a control sensor after addition of a fluid sample containing a constant concentration of ligand;

DRAWING DESC:

DRWD(3)

DRWD(3)

FIG. . . . calibration curve relating the initial rate of change of the conductance ratio to a known concentration of ligand in the fluid sample.

DRAWING DESC:

DRWD(4)

FIG. 2A shows the change in the conductance ratio in a fluid sample in which the ligand concentration varies with time; FIG. 2B shows the change in conductance ratio after a fluid sample pulse.

DRAWING DESC:

DRWD(9)

FIG. 5A shows typical apparatus used in determining the presence of a ligand in a fluid sample;

DRAWING DESC:

DRWD(12)

FIG. . . . sensor apparatus with several test cells and a negative and positive control, each cell having its own electric path and fluid path;

DRAWING DESC:

DRWD(13)

FIG. 6B shows a multiple sensor apparatus with cells in series, all cells sharing a common current path and fluid path.

DRAWING DESC:

DRWD(24)

FIG. 15 is a schematic diagram showing further details of the comparator circuit of FIG. 14.

DETDESC:

DETD(4)

Antiligand means substance used to probe for the presence of a ligand that specifically binds to the ligand.

DETDESC:

DETD(8)

Contacting means is the means used to insure contact between the localizing means and liquid sample containing the ligand of interest.

DETDESC:

DETD(17)

This invention relates to methods, apparatus and sensors for determining the presence of a ligand in a liquid sample by measuring ligand-induced changes in bulk electrical conductance.

DETDESC:

DETD(18)

In . . . embodiment, antiligand to the ligand of interest is localized within a predetermined region. The predetermined region is exposed to the liquid sample to be analyzed, and the bulk conductance of a volume (the test volume) that at least partially contains the. . . a result of

DETD(18)
ligand-antiligand interaction in the predetermined region may be used to determine the presence of ligand in the liquid sample.

DETDESC:

DETD(20)

Although the present methods and apparatus are designed to detect the presence of a ligand in a liquid sample, they are readily modified to detect the presence of a ligand in a gas, e.g., by dissolving or bubbling the gas through an appropriate liquid, or in a solid, e.g. by dissolving the solid in an appropriate liquid.

DETD(20)

DETDESC:

DETD(22)

Changes . . . or less). Large nonspecific changes in conductance can arise from local environment variations, for example, in temperature, composition of the liquid sample, viscosity changes, or non-specific binding of proteins or other substances to the predetermined region or test volume. These changes. . .

DETDESC:

DETD(23)

In . . . and quantify accurately the ligand-specific conductance change

one compares the bulk conductance of a test volume with the bulk conductance of at least one control volume. Both positive and. . .

DETDESC:

DETD(24)

In . . . preferred embodiment the negative control volume at least partially contains at least one predetermined region that is exposed to the fluid sample, and this predetermined region has localized in it a

DETD(24)

molecule whose physical properties are similar to the physical properties. . .

DETDESC:

DETD(25)

The conductance of a test volume can be compared with that of a negative control volume in various ways. For example, the value of each conductance may be measured, then that of the negative control subtracted from that of the test volume manually. . . of time, using the conductance ratio C, where ##EQU1## The test volume and/or the negative control volume can be further compared with a positive control volume. In this case a

DETD(25)

positive control ligand is present in known concentration in the fluid sample, and the positive control volume at least partially contains a predetermined region which itself has localized within it an antiligand which reacts with the positive control ligand. The test volume and the positive control volume may be compared to the negative control volume to correct for non-specific conductance changes, then to each other. The positive control signal can. . .

DETDESC:

DETD(26)

Localization . . . antiligands may be bound to different predetermined

DETD(26)

regions of matrix material, allowing multiple ligands to be detected in a single fluid sample.

DETDESC:

DETD(28)

The fluid sample and the predetermined region may be brought into contact in a variety of ways as described in more detail herein below. For example, a flowing stream of sample fluid may be contacted with the matrix of the predetermined region. The fluid may flow either through the matrix or past the matrix with diffusion carrying the ligand of interest into the matrix.

DETD(38)
For . . . binding, the amount of ligand bound per unit time will be proportional both to the concentration of ligand in the fluid sample and to the flow rate. This yields a high affinity, or kinetic, measure of ligand. For example, if the. . .

DETDESC:

DETD(39)

The observed value of the slope dC/dT will depend not only on the concentration of the particular ligand in the fluid sample and the flow rate, but also on other particulars of the experiment set-up, such as (1) the pore size of the predetermined region; (2) the total volume of fluid in

DETD(39)
the bioregion available for ion flow; (3) the efficiency E of the sensors, (4) the effective size of the. . . set of experimental conditions used. Once this is done, however, the presence and concentration of ligand in an unknown sample fluid may be determined by reference to the standard curve.

DETDESC:

DETD(41)

Various . . . be designed to maintain a constant, known flow rate throughout the course of a measurement, e.g., through use of appropriate fluid resistors and/or a peristaltic pump. Flow may be measured by

DETD(41)
various commercially available devices (e.g., a G-1000 microliter per minute flow meter with regulator valve, from Gilmont Instruments, Great Neck, NY). For particular sample fluids and ligands the change is conductance of a matrix due to both specific and non-specific binding of material from the fluid sample may well be correlated in a known way with the change in flow rate through the filter at a given applied pressure, since both changes may arise from common causes such as the binding of material from the fluid sample. The conductance ratio itself may sometimes thus be used as a measure of flow rate.

DETDESC:

DETD(42)

Referring now to FIG. 2A, if the ligand concentration in the fluid passing through the predetermined region varies with time, the slope dC/dt will vary with time. For example, at point 17, the ligand concentration in the fluid passing through the apparatus is significant, and as a result, the conductance ratio de[illegible]ases at a significant rat[illegible]as ligand. . .

DETDESC:

DETD(28)

DETDESC:

DETD(29)

Where the predetermined region comprises antiligand confined within a semi-permeable membrane, fluid is caused to flow past the membrane. The ligand diffuses through the membrane into the predetermined region.

DETDESC:

DETD(33)

DETD(33)

Antiligands . . . the concentration of free ligand needed to saturate half the antiligand binding sites at equilibrium (as long as the total number of ligand molecules is much is larger than the number of binding sites). When the affinity is high, the affinity constant is low, and vice versa. More specifically, antibodies with. . . are typically defined situationally: An antiligand is considered high affinity when the concentration of the ligand of interest in the fluid sample is much higher than the affinity constant, and low affinity otherwise. While not wishing to be bound by theory,. . .

DETDESC:

DETD(35)

Thus, . . . of dissociation r.sub.2 of ligand/antiligand complex may be ignored, and the association of ligand and antiligand is essentially irreversible. As fluid sample passes through the matrix in such a situation, binding is substantially quantitative as long as the fluid passes through the matrix slowly enough and a significant fraction of the binding sites are available; that is, virtually 100% of the ligand binds to immobilized antiligand and is removed from the fluid sample. In practice, the flow rate needed for quantitative binding depends on the reaction conditions such as salt concentration, temperature,. . .

DETDESC:

DETD(36)

Binding need not be quantitative. In some cases it may be appropriate to pass fluid through the predetermined region at a rate that does not give time for quantitative binding. In such a case it. . . be satisfactory to know the percent of binding which occurs, even if this is not 100%. In an extreme case, fluid will be passed through the predetermined region so quickly that only a small portion of the ligand entering the predetermined. . .

DETDESC:

DETD(38)

DETD(43)

Sample liquid may also be contacted with the predetermined region in a pulsed fashion resulting in a curve such as that shown in FIG. 2B. For

DETD(43)
example, liquid sample may be injected into a flowing buffer stream of the same conductivity using standard commercial valve equipment (e.g. Rheodyne. . .

DETDESC:

DETD(44)

As . . . ligand. Such a situation can arise, for example where the ligand of interest is present in high concentration in the liquid sample, e.g. 10.sup.-3 M, and it is desirable to monitor the concentration of ligand continuously over an extended period of. . . antiligand whose affinity constant K typically is within an order of magnitude of the concentration of

DETD(44)
ligand expected in the liquid sample, i.e., a low affinity situation. In this situation, the rate of dissociation r.sub.2 of ligand/antiligand complex is significant compared to the rate of association r.sub.1 (i.e., binding is reversible), and a significant fraction of the binding sites are unoccupied. . . 3A can thus be used as a standard curve to determine the presence or concentration of a ligand in a liquid sample. The dynamic range of such low affinity, or equilibrium, methods can be increased if desired by using several predetermined. . .

DETDESC:

DETD(45)

DETD(45)
Referring . . . shown an example of the use of low affinity antiligand in the detection of varying concentrations of ligand in a liquid sample. When the concentration of ligand in the liquid sample passing through the sensor rises (16), the conductance ratio falls as ligand binds to and occupies space in the. . . little or no ligand remains bound to the predetermined region, and the conductance ratio hence approaches or equals its original value. Later still, the ligand concentration rises again (20), reaches a new high (27), then falls again (22).

DETDESC:

DETD(49)

DETD(49)
The . . . method is inversely proportional to the volume of the

The . . . the fuel is injected and burned. One of the characteristics of the combustor 108 is that it delivers the heat value contained in the injected fuel to the air flowing through the combustor 108 with a high degree of efficiency and. . .

DETDESC:

DETD(87)

The . . . boost phase. At separation of the booster rocket 500 and missile 100, the missile will be travelling at a Mach number where, after rapid ignition of the fuel takes place, sufficient thrust for acceleration will be produced by the ramjet engine.. . .

DETDESC:

DETD(103)

The . . . 524 that are provided in the longitudinal feeder channels 480 and 482. To facilitate easy installation and to minimize the number of openings on the bladders, each bladder 438 has bonded to it two longitudinal

DETD(103)

tongues 526, the free ends of which are provided with a series of snap fastener holes corresponding to the number of snap fastener holes 524 in the longitudinal feeder channels 480 and 482. The bladders 438 conform to the inside. . .

DETDESC:

DETD(109)

When fully extended, the bladders 438 are supported by the walls of the fuel tank 138, except for a considerable number of holes in the various members 476, 478, 484, and 486 in the fuel tank structure. The bladders 438 conform. . .

DETD(109)

DETDESC:

DETD(133)

For flight of the missile 100 at maximum Mach number, the air pressure of the diffuser inlet of the turbine fuel pump 440 is sufficient to prevent cavitation during missile operation below 19,000 feet altitude. For minimum flight Mach number, the diffuser air pressure is sufficient below 8,000 feet altitude. Since the nitrogen supply is rapidly used up in low. . .

DETDESC:

DETD(153)

The . . . 774. The air

safety and arming device 132, a guidance system compartment 134, and a cover.
. .

DETDESC:

US PAT NO: 3,908,933 [IMAGE AVAILABLE] L10: 4 of 4

DETD(26)

Each wing has a high aspect ratio and tip rake, which tends to minimize hinge moment variations with Mach number under various combinations of wing deflection and missile angle of attack with the tapered planform of each wing tending to. . .

DETDESC:

DETD(39)

Each winglock 140 comprises a housing having located therein a piston (not shown) which is actuated by hydraulic fluid applied through the tube 395. The piston drives a rod 397, one end 399 of which is received in a. . .

US PAT NO: 3,908,933 [IMAGE AVAILABLE] L10: 4 of 4

DETD(39)

DETDESC:

DETD(61)

FIG. . . . or more angle shock steps before it reaches the final weak normal shock that drops the velocity to a subsonic value. The normal shock, in this case is much less severe than one across an open duct. Using this method, therefore,. . .

DETDESC:

US PAT NO: 3,908,933 [IMAGE AVAILABLE] L10: 4 of 4

DETD(62)

Assuming that the ramjet engine has been boosted to a Mach number M = 1.7, a cycle through the engine will be followed by reference to FIGS. 92, 93, 94 and 95.. . .

DETDESC:

DETD(70)

The . . . is comprised of a Ferri type inlet designed for high pressure recovery with low additive drag over the design Mach number range, a cylindrical section, and a conical-cylindrical section which encloses the combustor pilot 320, FIGS. 1 and 7.

US PAT NO: 3,908,933 [IMAGE AVAILABLE] L10: 4 of 4

DETD(70)

DETDESC:

DETD(75)

DETD(61)

DETDESC:

DETD(62)

Particles . . . No. 4,376,110) is easily derived: A monoclonal antibody specific for an extended antigen is immobilized, e.g. on a nitrocellulose filter. Fluid sample containing the antigen is exposed to the filter, allowing antigen to bind. Then a second, non-interfering monoclonal antibody specific. . . .

DETDESC:

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

DETD(63)

In . . . with antiligand to the ligand of interest if localized within a predetermined region. The predetermined region is exposed to the fluid sample and also to an antiligand which interacts both with the ligand in the fluid sample and with ligand localized in the predetermined region. The bulk conductance of a test volume that at least partially. . . .

DETDESC:

DETD(64)

As . . . previously described embodiment wherein antiligand is localized in the predetermined region, the bulk conductance of the test volume may be
=> d l10 4 kwic

US PAT NO: 3,908,933 [IMAGE AVAILABLE] L10: 4 of 4

US PAT NO: 3,908,933 [IMAGE AVAILABLE] L10: 4 of 4

DRAWING DESC:

DRWD(72)

FIG. 71 is a section through the probe static relief valve of the fuel system;

DETDESC:

DETD(9)

The airframe assembly for the missile 100 is comprised of a number of major assemblies for ease of manufacturing and assembly, namely a forward body assembly 102 (including a nose section 104),. . .

US PAT NO: 3,908,933 [IMAGE AVAILABLE] L10: 4 of 4

DETD(9)

DETDESC:

DETD(10)

The . . . assembly 1[illegible] includes an inner body 12[illegible] including an accumulator 122, homing antennae 124 and waveguide 125, a static pressure probe 126, a ram pressure probe 128, [illegible]

In . . . the basis of another type of particle-enhanced competitive conductance assay. It may be used to continuously monitor ligand in a fluid sample. Compartment 26 may be formed, for example, by confining complex 24 within a semipermeable membrane 32 that is permeable to the ligand of interest. When the sample fluid contains no free ligand, complex 24 will tend to lie within the test volume, since it will bind to the antiligand in the predetermined region. When the sample fluid contains a high level of the ligand, many complexes 24 will lie outside test volume 30, changing the conductance of the test volume, since they will be competed off predetermined region 28 by the ligand in the fluid sample and will be free to move through compartment 26. The ligand/particle complex 24 may bind only to the surface. . .

30 SEP 91 08:23:17 U.S. Patent & Trademark Office P0099

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

DETD(56)

DETDESC:

DETD(58)

More . . . and predetermined region 28 and competes with particle complex 24 for antiligand binding sites. When the ligand concentration in the fluid sample is low, most of complex 24 is bound to the predetermined region 28. When it is high, most of. . . measuring the conductance of the test volume can be used to determine the presence and concentration of ligand in the fluid sample.

30 SEP 91 08:23:25 U.S. Patent & Trademark Office P0100

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

DETD(58)

DETDESC:

DETD(60)

Similarly, . . . used to influence the ability of particles to stick to a surface. For example, one could remove particles from a fluid sample while measuring the amount of ligand present by passing the sample rapidly past a filter containing immobilized antiligand; if. . . from the filter and also will be prevented from piling up on the filter by the "sweeping" action of the fluid flowing tangentially over the surface. Particle-free fluid carrying ligand can meanwhile pass through the filter, allowing binding of ligand to the immobilized antiligand. On the other hand,. . .

30 SEP 91 08:23:35 U.S. Patent & Trademark Office P0101

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

DETD(60)

DETDESC:

DETD(61)

Conductance . . . a known amount of antiligand and particles are incubated to form a preformed complex. This complex is added to the fluid sample. Ligand in the sample binds to antiligand in the complex and also to antiligand localized in the predetermined region. The number of particles bound to the predetermined region depends on the amount of free ligand in the sample. This gives a. . .

30 SEP 91 08:23:44 U.S. Patent & Trademark Office P0102

US PAT NO: 4,713,347 [IMAGE AVAILABLE] L10: 3 of 4

total number of binding sites (assuming a defined fraction of predetermined region by weight is antiligand); thus, the larger the number of ligand molecules required to result in a given fraction of occupied binding sites. Therefore, where sample size is limited. . .

DETDESC:

DETD(50)

As an example, suppose that one ml of a fluid sample containing 1 ug/ml ligand flows through a sensor, the volume of whose predetermined region is

DETD(50)
about one microliter, with. . .

DETDESC:

DETD(53)

The simplest use of a particle for enhancing the change in bulk conductance is where ligand in the fluid sample is directly bound to particles by incubation. The ligand/particle complex in the fluid sample is then exposed to the predetermined region, yielding a larger signal as ligand/particle complexes bind than if ligand alone. . . In a variation of the above, a known amount of ligand that interacts with antiligand may be added to the fluid sample. This ligand can compete with ligand/particle

DETD(53)
complexes for antiligand, thus forming the basis for a competitive particle-enhanced conductance assay.

DETDESC:

DETD(54)

In . . . of a known ligand that interacts with antiligand is first bound to particles and this comlex is added to the fluid sample; ligand from the fluid sample can then compete with this ligand/particle complex, forming another type of particle-enhanced competitive conductance assay.

DETD(54)

DETDESC:

DETD(55)

In . . . and a particle, and the complex is allowed to bind to the region. This region is then exposed to sample fluid containing ligand, which can compete off the ligand/particle complex. In a variation of this technique, the ligand/particle complexes released from. . .

DETDESC:

DETD(56)